Assay Weigh accurately about 0.5 g of Diclofenac Sodium, previously dried, dissolve with 40 mL of water in a separator, add 2 mL of dilute hydrochloric acid, and extract the precipitate formed with 50 mL of chloroform. Extract again with two 20-mL portions of chloroform, and filter the extract each time through a pledget of absorbent cotton moistened with chloroform. Wash the tip of the separator and the absorbent cotton with 15 mL of chloroform, combine the washing with the extracts, add 10 mL of a solution of 1 mol/L hydrochloric acid TS in ethanol (99.5) (1 in 100), and titrate with 0.1 mol/L potassium hydroxide-ethanol VS from the first equivalent point to the second equivalent point (potentiometric titration).

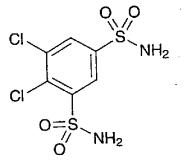
Each mL of 0.1 mol/L potassium hydroxide-ethanol VS
= 31.813 mg of $C_{14}H_{10}Cl_2NNaO_2$

Containers and storage Containers—Tight containers.

Diclofenamide

Dichlorphenamide

ジクロフェナミド



$C_6H_6Cl_2N_2O_4S_2$: 305.16
4,5-Dichlorobenzene-1,3-disulfonamide [*120-97-8*]

Diclofenamide, when dried, contains not less than 98.0% of $C_6H_6Cl_2N_2O_4S_2$.

Description Diclofenamide occurs as a white, crystalline powder.

It is very soluble in *N,N*-dimethylformamide, soluble in ethanol (95), and very slightly soluble in water.

It dissolves in sodium hydroxide TS.

Identification **(1)** Dissolve 0.01 g of Diclofenamide in 100 mL of 0.01 mol/L sodium hydroxide TS. To 10 mL of the solution add 0.1 mL of hydrochloric acid. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Diclofenamide Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Diclofenamide, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Diclofenamide Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

Melting point 237 - 240°C

Purity **(1)** Chloride—Dissolve 0.10 g of Diclofenamide in 10 mL of *N,N*-dimethylformamide, and add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.45 mL of 0.01 mol/L hydrochloric acid VS add 10 mL of *N,N*-dimethylformamide, 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.160%).

(2) Selenium—To 0.10 g of Diclofenamide add 0.5 mL of a mixture of perchloric acid and sulfuric acid (1:1) and 2 mL of nitric acid, and heat on a water bath until no more brown gas evolves and the solution becomes to be a light yellow clear solution. After cooling, add 4 mL of nitric acid to this solution, then add water to make exactly 50 mL, and use this solution as the sample solution. Separately, pipet 3 mL of Standard Selenium Solution, add 0.5 mL of a mixture of perchloric acid and sulfuric acid (1:1) and 6 mL of nitric acid, then add water to make exactly 50 mL, and use this solution as the standard solution. Perform the test with the sample solution and the standard solution as directed under the Atomic Absorption Spectrophotometry according to the following conditions, and determine constant absorbances, A_T and A_S, obtained on a recorder after rapid increasing of the absorption: A_T is smaller than A_S (not more than 30 ppm).

Perform the test by using a hydride generating system and a thermal absorption cell.

Lamp: An selenium hollow cathode lamp

Wavelength: 196.0 nm

Temperature of sample atomizer: When an electric furnace is used, about 1000°C.

Carrier gas: Nitrogen or Argon

(3) Heavy metals—Proceed with 2.0 g of Diclofenamide according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(4) Related substances—Dissolve 0.10 g of Diclofenamide in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 2 mL of the sample solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of these solutions by the automatic integration method: the total area of the peaks other than the peak of diclofenamide from the sample solution is not larger than the peak area of diclofenamide from the standard solution.

Operating conditions—

Detector, column, column temperature, mobile phase, flow rate, and selection of column: Proceed as directed in the operating conditions in the Assay.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of diclofenamide obtained from 10 μL of the standard solution is between 5 mm and 10 mm.

Time span of measurement: About 5 times as long as the retention time of diclofenamide.

Loss on drying Not more than 1.0% (1 g, in vacuum at a pressure not exceeding 0.67 kPa, 100°C, 5 hours).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.05 g each of Diclofenamide and Diclofenamide Reference Standard, previous-

ly dried, and dissolve each in 30 mL of the mobile phase. To each add exactly 10 mL of the internal standard solution and the mobile phase to make 50 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of diclofenamide to that of the internal standard, respectively.

Amount (mg) of $C_6H_6Cl_2N_2O_4S_2$
= amount (mg) of Diclofenamide Reference Standard
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of butyl parahydroxy benzoate in the mobile phase (3 in 5000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: A mixture of sodium phosphate TS and acetonitrile (1:1).

Flow rate: Adjust the flow rate so that the retention time of diclofenamide is about 7 minutes.

Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of diclofenamide and the internal standard in this order with the resolution between these peaks being not less than 9.

Containers and storage Containers—Tight containers.

Diclofenamide Tablets

Dichlorphenamide Tablets

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Diclofenamide Tablets contain not less than 92% and not more than 108% of the labeled amount of diclofenamide ($C_6H_6Cl_2N_2O_4S_2$: 305.16).

Method of preparation Prepare as directed under Tablets, with Diclofenamide.

Identification To a quantity of powdered Diclofenamide Tablets, equivalent to 0.2 g of Diclofenamide according to the labeled amount, add 20 mL of methanol, shake, and filter. Evaporate the filtrate on a water bath to dryness, and dissolve 0.01 g of the residue in 100 mL of 0.01 mol/L sodium hydroxide TS. To 10 mL of this solution add 0.1 mL of hydrochloric acid TS, and determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 284 nm and 288 nm, and between 293 nm and 297 nm.

Dissolution test Perform the test with 1 tablet of Diclofenamide Tablets at 50 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of water as the test solution. Take 20 mL or more of the dissolved solution 60 minutes after starting the test, and filter through a membrane filter with pore size of not more than 0.8 μm. Discard the first 10 mL of the filtrate, and use the subsequent as the sample solution. Separately, weigh accurately about 0.055 g of Diclofenamide Reference Standard, previously dried in vacuum at a pressure not exceeding 0.67 kPa at 100°C for 5 hours, dissolve in 10 mL of methanol, and add water to make exactly 100 mL. Pipet 10 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and the standard solution at 285 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Diclofenamide Tablets in 60 minutes is not less than 70%.

Dissolution rate (%) with respect to
the labeled amount of diclofenamide ($C_6H_6Cl_2N_2O_4S_2$)
$= W_S \times \frac{A_T}{A_S} \times \frac{1}{C} \times 90$

W_S: Amount (mg) of Diclofenamide Reference Standard.
C: Labeled amount (mg) of diclofenamide ($C_6H_6Cl_2N_2O_4S_2$) in 1 tablet.

Assay Weigh accurately, and powder not less than 20 tablets of Diclofenamide Tablets. Weigh accurately a portion of the powder, equivalent to about 0.05 g of diclofenamide ($C_6H_6Cl_2N_2O_4S_2$), add exactly 25 mL of the mobile phase, shake for 15 minutes, and centrifuge. Pipet 10 mL of the supernatant liquid, add exactly 4 mL of the internal standard solution and the mobile phase to make 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of Diclofenamide Reference Standard, previously dried at 100°C in vacuum at a pressure not exceeding 0.67 kPa for 5 hours, dissolve in 30 mL of the mobile phase, add exactly 10 mL of the internal standard solution and the mobile phase to make 50 mL, and use this solution as the standard solution. Proceed as directed in the Assay under Diclofenamide.

Amount (mg) of diclofenamide ($C_6H_6Cl_2N_2O_4S_2$)
= amount (mg) of Diclofenamide Reference Standard
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of butyl parahydroxybenzoate in the mobile phase (3 in 5000).

Containers and storage Containers—Well-closed containers.